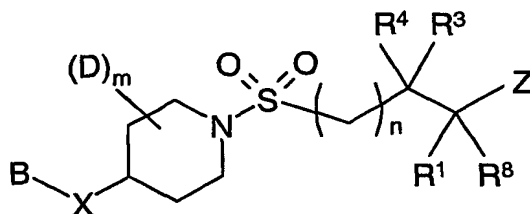


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CLAIMS:

What we claim is :-

1. A compound of formula (1):



formula (1)

wherein Z is selected from $-\text{CONR}^{15}\text{OH}$ and $-\text{N}(\text{OH})\text{CHO}$;

R^{15} is hydrogen or C_{1-3} alkyl;

wherein R^1 is hydrogen or a group selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{5-7} cycloalkenyl, aryl, heteroaryl and heterocyclyl where the group is optionally

- substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl (optionally substituted by one or more R^{17}), aryl (optionally substituted by one or more R^{17}), heteroaryl (optionally substituted by one or more R^{17}), heterocyclyl, C_{1-4} alkoxycarbonyl, $-\text{OR}^5$, $-\text{SR}^2$, $-\text{SOR}^2$, $-\text{SO}_2\text{R}^2$, $-\text{COR}^2$, $-\text{CO}_2\text{R}^5$, $-\text{CONR}^5\text{R}^6$, $-\text{NR}^{16}\text{COR}^5$, $-\text{SO}_2\text{NR}^5\text{R}^6$ and $-\text{NR}^{16}\text{SO}_2\text{R}^2$;

R^{16} is hydrogen or C_{1-3} alkyl;

R^{17} is selected from halo, C_{1-6} alkyl, C_{3-6} cycloalkyl and C_{1-6} alkoxy;

R^2 is group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl where the group is optionally substituted by

- one or more halo;

R^5 is hydrogen or a group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, heterocycloalkyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl where the group is

optionally substituted by one or more halo;

R^6 is hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl;

- or R^5 and R^6 together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

wherein R^8 is hydrogen or a group selected from C_{1-6} alkyl, C_{3-7} cycloalkyl and heterocyclyl

where the group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy and C_{1-4} alkyl;

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or R¹ and R⁸ together form a carbocyclic or saturated heterocyclic 3- to 6-membered ring;
wherein R³ and R⁴ are independently hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₅₋₇cycloalkenyl,
heterocyclyl, aryl or heteroaryl;

wherein n is 0 or 1;

5 wherein m is 0 or 1;

wherein D is hydrogen, C₁₋₄alkyl, C₃₋₆cycloalkyl or fluoro;

wherein X is $-(CR^9R^{10})-Q-(CR^{11}R^{12})_u-$ where u is 0 or 1;

Q is O, S, SO or SO₂;

R⁹, R¹⁰, R¹¹ and R¹² are independently selected from hydrogen, C₁₋₄alkyl and C₃₋₆cycloalkyl;

10 wherein B is C₂₋₄alkenyl or C₂₋₄alkynyl, each being optionally independently substituted by a
group selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, heterocycloalkyl, aryl, heteroaryl, heterocyclyl
whereby the group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl,
trifluoromethoxy, $-\text{CONHR}^{13}$, $-\text{CONHR}^{13}\text{R}^{14}$, $-\text{SO}_2\text{R}^{13}$, $-\text{SO}_2\text{NHR}^{13}$, $-\text{SO}_2\text{NR}^{13}\text{R}^{14}$, $-\text{NHSO}_2\text{R}^{13}$, C₁₋₄alkyl and C₁₋₄alkoxy;

15 R¹³ and R¹⁴ are independently hydrogen, C₁₋₄alkyl or C₃₋₅cycloalkyl;

or R¹³ and R¹⁴ together with the nitrogen to which they are attached form a heterocyclic 4 to
7-membered ring.

or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof.

20 2. A compound according to claim 1 wherein X is $-(\text{CH}_2)-\text{O}-$ or $-(\text{CH}_2)-\text{O}-(\text{CH}_2)-$.

3. A compound according to claim 1 or 2 wherein B is C₂₋₄alkenyl or C₂₋₄alkynyl, each
being optionally independently substituted by C₁₋₄alkyl, C₃₋₆cycloalkyl, aryl, heteroaryl or
heterocycloalkyl.

25

4. A compound according to any one of claims 1 to 3 wherein R¹ is hydrogen, C₁₋₆alkyl
or aryl where C₁₋₆alkyl or aryl are optionally substituted by one or more substituents
independently selected from C₁₋₄alkyl, aryl (optionally substituted by R¹⁷) and heteroaryl
(optionally substituted by R¹⁷) and wherein R¹⁷ is halo or C₁₋₄alkyl.

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5. A compound according to any one of claims 1 to 4 for use as a medicament.

6. The use of a compound according to any one of claims 1 to 4 in the manufacture of a
5 medicament in the treatment of a disease condition mediated by one or more metalloproteinase enzymes.

7. The use of a compound according to any one of claims 1 to 4 in the manufacture of a medicament in the treatment of a disease condition mediated TNF α .

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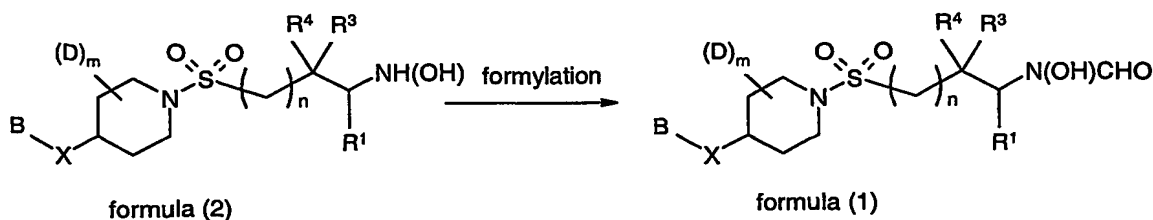
8. A method of treating autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a compound according to claim 1.

15

9. A pharmaceutical composition comprising a compound according to any one of claims 1 to 4; and a pharmaceutically-acceptable diluent or carrier.

10. A process for preparing a compound according to claim 1 comprising, when Z is –
20 N(OH)CHO, the step of:

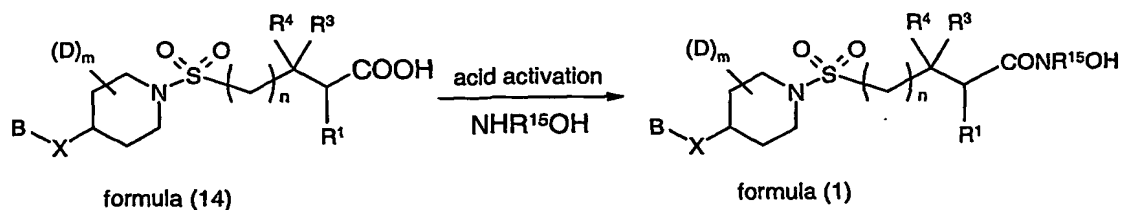
a) converting a hydroxylamine of formula (2) into a compound of formula (1);



or when Z is $-CONR^{15}OH$, the step of:

25 b) converting an acid of formula (14) into a compound of formula (1);

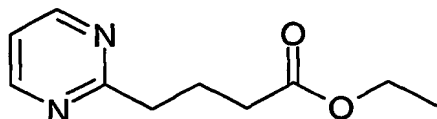
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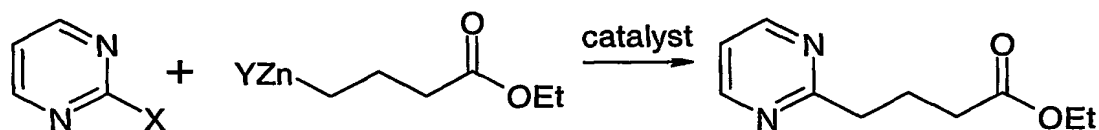
and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;
- 5 iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.

11. Ethyl 4-(pyrimidin-2-yl)butanoate.



- 10 12. A process comprising the reaction of a 2-halopyrimidine, 2-tosylpyrimidine, 2-pyrimidinyl triflate or 2-pyrimidinyl mesylate with 4-ethoxy-4-oxo-butylzinc bromide or 4-ethoxy-4-oxo-butylzinc iodide in the presence of a catalyst;



wherein X is halo, triflate or mesylate and Y is bromide or iodide.

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13. A process according to claim 11 wherein the catalyst is generated from bis(acetonitrile) palladium (II) dichloride and triphenylphosphine.

14. The use of bis(acetonitrile) palladium (II) dichloride and triphenylphosphine in a
20 Negishi coupling reaction.